IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Jane Hirsh, Roman V. Rariy, and Michael Heffernan

Serial No.: 10/690,872 Art Unit: Not Yet Assigned

Filed: October 22, 2003 Examiner: Not Yet Assigned

For: *PULSATILE RELEASE COMPOSITIONS OF MILNACIPRAN*

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT

Sir:

Pursuant to 37 C.F.R. §1.56 and 37 C.F.R. §1.97, Applicants submit an Information Disclosure Statement, including eighteen (18) pages of Form PTO-1449 and a copy of each document cited therein.

This Information Disclosure Statement is being filed under 37 C.F.R. § 1.97(b) prior to a first Office Action on the merits. It is believed that no fee is required with this submission. However, should a fee be required, the Commissioner is hereby authorized to charge any required fees to Deposit Account No. 50-1868.

U.S. Patents

Number	Issue Date	Patentee	Class/Subclass
3,948,254	04-06-1976	Zaffaroni	128/127
3,977,992	08-31-1976	Hofacker	252/316
4,069,307	01-17-1978	Higuchi, et al.	424/22
4,093,709	06-06-1978	Choi, et al.	424/19
4,122,157	10-24-1978	Huber	424/21
4,138,475	02-06-1979	McAinsh, et al.	424/19

4,142,526	03-06-1979	Zaffaroni	128/260
4,173,626	11-06-1979	Dempski	424/19
4,226,849	10-07-1980	Schor	424/19
4,249,531	02-10-1981	Heller, et al.	128/260
4,252,786	02-24-1981	Weiss, et al.	424/19
4,264,573	04-28-1981	Powell, et al.	424/19
4,304,232	12-08-1981	Michaels	128/260
4,308,251	12-29-1981	Dunn, et al.	424/19
4,322,311	05-30-1982	Lim, et al.	252/316
4,346,709	08-31-1982	Schmitt	128/260
4,353,887	10-12-1982	Hess, et al.	424/15
4,367,741	01-11-1983	Michaels	128/260
4,415,547	11-15-1983	Yu, et al.	424/19
4,428,925	01-31-1984	Keith	424/19
4,428,926	01-31-1984	Keith	424/19
4,432,965	02-21-1984	Keith, et al.	424/19
4,455,144	06-19-1984	Michaels	604/892
4,478,836	10-23-1984	Mouzin, et al.	424/248.54
4,482,533	11-13-1984	Keith	421/28
4,503,031	03-05-1985	Glassman	424/15
4,505,890	03-19-1985	Jain, et al.	424/21
4,508,702	04-02-1985	Hsiao	424/19
4,520,009	05-28-1985	Dunn	424/78
4,524,060	06-18-1985	Mughal, et al.	424/19
4,540,566	09-10-1985	Davis, et al.	424/22
4,556,678	12-03-1985	Hsiao	514/652
4,557,925	21-10-1985	Lindahl, et al.	424/19
4,571,333	02-18-1986	Hsiao, et al.	424/22
4,587,118	05-06-1986	Hsiao	424/19
4,610,870	09-09-1986	Jain, et al.	424/19
4,629,619	12-16-1986	Lindahl, et al.	424/15
4,629,620	12-16-1986	Lindahl, et al.	424/15
4,634,587	01-06-1987	Hsiao	424/19
4,649,043	03-10-1987	Urquhart, et al.	424/469
4,666,705	05-19-1987	DeCrosta, et al.	424/482
4,690,824	09-01-1987	Powell, et al.	424/468
4,692,337	09-08-1987	Ukigaya	424/469
4,695,467	09-22-1987	Uemura, et al.	424/502
4,695,591	09-22-1987	Hanna, et al.	514/781
4,708,834	11-24-1987	Cohen, et al.	264/4.3
4,710,384	12-01-1987	Rotman	424/465
4,734,285	03-29-1988	Alderman	424/468
4,740,198	04-26-1988	Theeuwes	604/84
4,756,911	07-12-1988	Drost, et al.	424/468
4,775,535	10-04-1988	Lowey	424/468

4,781,919	11-01-1988	Liebowitz	424/78
4,784,858	11-15-1988	Ventouras	424/468
4,795,327	01-03-1989	Gaylord, et al.	424/468
4,795,642	01-03-1989	Cohen, et al.	424/455
4,795,645	01-03-1989	Friedman, et al.	424/468
4,798,725	01-17-1989	Patel	424/456
4,800,083	01-24-1989	Hom, et al.	424/457
4,803,076	02-07-1989	Ranade	424/438
4,803,079	02-07-1989	Hsiao, et al.	424/468
4,806,359	02-21-1989	Radebaugh, et al.	424/470
4,816,262	03-28-1989	McMullen	424/467
4,820,522	04-11-1989	Radebaugh, et al.	424/468
4,822,619	04-18-1989	Eichel, et al.	424/492
4,824,678	04-25-1989	Lindahl, et al.	424/473
4,832,957	05-23-1989	Dempski, et al.	424/469
4,837,032	06-06-1989	Ortega	424/469
4,842,866	06-27-1989	Horder, et al.	424/468
4,849,229	07-18-1989	Gaylord, et al.	424/468
4,861,590	08-29-1989	Grodberg	424/602
4,863,743	09-05-1989	Hsiao, et al.	424/476
4,871,548	10-03-1989	Edgren, et al.	424/488
4,882,167	11-21-1989	Jang	424/468
4,892,742	01-09-1990	Shah	424/480
4,900,755	02-13-1990	Dempski, et al.	424/469
4,919,938	04-24-1990	Lovegrove, et al.	424/480
4,925,676	05-15-1990	Ghebre-Sellassie	424/470
4,933,185	06-12-1990	Wheatley, et al.	424/461
4,946,686	08-07-1990	McClelland, et al.	424/473
4,956,388	09-11-1990	Robertson, et al.	514/651
4,966,768	10-30-1990	Michelucci, et al.	424/468
4,968,509	11-06-1990	Radebaugh, et al.	424/470
4,983,398	01-08-1991	Gaylord, et al.	424/465
4,983,400	01-08-1991	Dempski, et al.	424/469
4,983,401	01-08-1991	Eichel, et al.	424/473
4,996,060	02-26-1991	Eckenhoff, et al.	424/473
5,002,774	03-26-1991	Agrawal, et al.	424/468
5,004,613	04-02-1991	Radebaugh, et al.	424/465
5,007,790	04-16-1991	Shell	424/451
5,009,895	04-23-1991	Lui	424/465
5,015,479	05-14-1991	Mulligan, et al.	424/457
5,019,398	05-28-1991	Daste	424/480
5,051,261	09-24-1991	McGinity, et al.	424/464
5,055,306	10-08-1991	Barry, et al.	424/482
5,057,318	10-15-1991	Magruder, et al.	424/438
5,073,380	12-17-1991	Babu, et al.	424/472

5,075,114	12-24-1991	Roche	424/470
5,085,865	02-04-1992	Nayak	424/472
5,091,189	02-25-1992	Heafield, et al.	424/457
5,112,614	05-12-1992	Magruder, et al.	424/422
5,126,145	06-30-1992	Evenstad, et al.	424/465
5,137,727	08-11-1992	Eckenhoff	424/422
5,162,117	11-10-1992	Stupak	424/475
5,164,193	11-17-1992	Okada, et al.	424/468
5,169,642	11-08-1992	Brinker, et al.	424/488
5,186,930	02-16-1993	Kogan, et al.	424/78.1
5,200,193	04-06-1993	Radebaugh, et al.	424/468
5,204,121	04-20-1993	Bücheler, et al.	424/495
5,219,572	06-15-1993	Sivaramakrishnan	424/438
5,230,901	06-27-1993	Einig, et al.	424/468
5,234,692	08-10-1993	Magruder, et al.	424/473
5,234,693	08-10-1993	Magruder, et al.	424/473
5,238,687	08-24-1993	Magruder, et al.	424/473
5,268,182	12-07-1993	Brinker, et al.	424/488
5,277,912	01-11-1994	Lowe, et al.	424/438
5,278,201	01-11-1994	Dunn, et al.	523/113
5,278,202	01-11-1994	Dunn, et al.	523/113
5,283,065	02-01-1994	Doyon, et al.	424/467
5,292,533	03-08-1994	McMahon, et al.	424/408
5,292,534	03-08-1994	Valentine, et al.	424/451
5,320,616	06-14-1994	Magruder, et al.	604/892.1
5,324,519	06-28-1994	Dunn, et al.	424/426
5,328,697	07-12-1994	Raman, et al.	424/477
5,334,392	08-02-1994	Cuine, et al.	424/468
5,334,393	08-02-1994	Bougaret, et al.	424/469
5,340,849	08-23-1994	Dunn, et al.	523/113
5,356,635	10-18-1994	Raman, et al.	424/484
5,358,723	10-25-1994	Ghebre-Sellassie	424/485
5,362,424	11-08-1994	Lee, et al.	264/4.3
5,366,738	11-22-1994	Rork, et al.	424/473
5,368,859	11-29-1994	Dunn, et al.	424/426
5,368,862	11-29-1994	Colegrove	424/464
5,393,765	02-28-1995	Infeld, et al.	514/365
5,397,574	03-14-1995	Chen	424/451
5,407,686	04-18-1995	Patel, et al.	424/468
5,413,572	05-09-1995	Wong, et al.	604/892.1
5,419,918	05-30-1995	Lundberg	424/490
5,424,289	06-13-1995	Yang, et al.	514/12
5,427,798	06-27-1995	Ludwig, et al.	424/464
5,427,799	06-27-1995	Valentine, et al.	424/451
5,433,951	06-18-1995	Serajuddin, et al.	424/486

5,455,046	10-03-1995	Baichwal	424/457
5,462,747	10-31-1995	Radebaugh, et al.	424/465
5,466,460	11-14-1995	McMahon, et al.	424/408
5,484,607	01-16-1996	Horacek	424/460
5,487,897	01-30-1996	Polson, et al.	424/426
5,492,700	02-20-1996	Ghebre-Sellassie	424/489
5,498,422	03-12-1996	Nakamichi, et al.	424/451
5,500,227	03-19-1996	Oshlack, et al.	424/476
5,505,962	04-09-1996	Sparks	424/473
5,508,041	04-16-1996	Lee, et al.	424/451
5,512,293	04-30-1996	Landrau, et al.	424/449
5,512,297	04-30-1996	Baichwal	424/451
5,540,912	07-30-1996	Roorda, et al.	424/422
5,543,155	08-06-1996	Fekete, et al.	424/473
5,554,387	09-10-1996	Baichwal	424/488
5,558,879	09-24-1996	Chen, et al.	424/480
5,562,915	10-08-1996	Lowe, et al.	424/438
5,576,021	09-19-1996	Andoh, et al.	424/468
5,578,321	11-26-1996	Sherman	424/453
5,582,837	12-10-1996	Shell	424/451
5,593,694	01-14-1997	Hayashida, et al.	424/468
5,599,552	02-04-1997	Dunn, et al.	424/423
5,601,842	02-11-1997	Bartholomaeus	424/464
5,603,956	02-18-1997	Mateescu, et al.	424/488
5,614,218	03-25-1997	Olsson, et al.	424/456
5,621,142	04-15-1997	Mochizuki, et al.	564/164
5,624,683	04-29-1997	Andoh, et al.	424/470
5,626,874	05-06-1997	Conte, et al.	424/464
5,630,808	05-20-1997	Magruder, et al.	604/892.1
5,643,602	07-01-1997	Ulmius	424/462
5,645,858	07-08-1997	Kotwal, et al.	424/495
5,650,170	07-22-1997	Wright, et al.	424/473
5,654,005	08-05-1997	Chen, et al.	424/480
5,656,291	08-12-1997	Olsson, et al.	424/458
5,660,837	08-26-1997	Lundquist	424/400
5,667,801	09-16-1997	Baichwal	424/457
5,681,582	10-28-1997	Gilis, et al.	424/468
5,681,583	10-28-1997	Conte, et al.	424/472
5,688,530	11-18-1997	Bodmer, et al.	424/501
5,690,960	11-25-1997	Bengtsson, et al.	424/480
5,702,716	12-30-1997	Dunn, et al.	424/422
5,705,190	01-06-1998	Broad, et al.	424/465
5,707,655	01-13-1998	Kanikanti, et al.	424/468
5,733,950	03-31-1998	Dunn, et al.	523/113
5,736,152	04-07-1998	Dunn	424/426

5,736,159	04-07-1998	Chen, et al.	424/480
5,739,176	04-14-1998	Dunn, et al.	523/113
5,744,153	04-28-1998	Yewey, et al.	424/426
5,759,563	06-02-1998	Yewey, et al.	424/426
5,776,489	07-07-1998	Preston, et al.	424/451
5,780,044	07-14-1998	Yewey, et al.	424/426
5,783,212	07-21-1998	Fassihi, et al.	424/472
5,846,563	12-08-1998	Baichwal	424/457
5,849,330	12-15-1998	Marvola, et al.	424/472
5,861,166	01-19-1999	Eckenhoff	424/422
5,869,100	02-09-1999	Horacek	424/488
5,874,107	02-23-1999	Fischer, et al.	424/464
5,879,707	03-09-1999	Cartilier, et al.	424/468
5,882,682	03-16-1999	Rork, et al.	424/473
5,885,615	03-23-1999	Chouinard, et al.	424/465
5,888,533	03-30-1999	Dunn	424/423
5,900,425	05-04-1999	Kanikanti, et al.	514/356
5,945,115	08-31-1999	Dunn, et al.	424/422
5,945,125	08-31-1999	Kim	424/473
5,980,942	11-09-1999	Katzhendler, et al.	424/465
5,990,194	11-23-1999	Dunn, et al.	523/113
6,010,718	01-04-2000	Al-Razzak, et al.	424/464
6,024,982	02-15-2000	Oshlack, et al.	424/476
6,027,748	02-22-2000	Conte, et al.	424/458
6,030,641	02-29-2000	Yamashita, et al.	424/451
6,030,642	02-29-2000	Horacek	424/457
6,033,685	03-07-2000	Qiu, et al.	424/464
6,033,686	03-07-2000	Seth	424/482
6,046,177	04-04-2000	Stella, et al.	514/58
6,056,977	05-02-2000	Bhagwat, et al.	424/488
6,066,643	05-23-2000	Perry	514/269
6,074,669	06-13-2000	Nagaprasad, et al.	424/458
6,077,538	06-20-2000	Merrill, et al.	424/470
6,083,533	07-04-2000	Cremer	424/472
6,090,411	07-18-2000	Pillay, et al.	424/468
6,093,387	07-25-2000	Birbara, et al.	424/76.7
6,099,859	08-08-2000	Cheng, et al.	424/464
6,099,862	08-08-2000	Chen, et al.	424/473
6,106,863	08-22-2000	Ukigaya, et al.	424/480
6,113,938	09-05-2000	Chen, et al.	424/423
6,120,789	09-19-2000	Dunn	424/426
6,126,967	10-03-2000	Clemente, et al.	424/461
6,136,343	10-24-2000	Baichwal	424/468
6,143,314	11-07-2000	Chandrashekar, et al.	424/426
6,143,353	11-07-2000	Oshlack, et al.	427/2.21

6,149,940	11-21-2000	Maggi, et al.	424/472
6,150,396	11-21-2000	Iyengar, et al.	514/438
6,150,410	11-21-2000	Engh, et al.	514/557
6,156,343	12-05-2000	Morita, et al.	424/474
6,162,463	12-19-2000	Lippa	424/451
6,162,466	12-19-2000	Licht, et al.	424/468
6,174,547	01-16-2001	Dong, et al.	424/463
6,180,129	01-30-2001	Magruder, et al.	424/422
6,197,339	03-06-2001	Ju	424/468
6,197,344	03-06-2001	Chang, et al.	424/489
6,210,714	04-03-2001	Oshlack, et al.	424/476
6,221,395	04-24-2001	Maggi, et al.	424/475
6,245,357	06-12-2001	Edgren, et al.	424/473
6,251,432	06-26-2001	Mazer, et al.	424/480
6,254,891	07-03-2001	Anaebonam, et al.	424/497
6,261,583	07-17-2001	Dunn, et al.	424/422
6,261,601	07-17-2001	Talwar, et al.	424/469
6,270,799	08-07-2001	Siefert, et al.	424/474
6,274,171	08-14-2001	Sherman, et al.	424/461
6,284,275	09-04-2001	Chen, et al.	424/473
6,303,144	10-16-2001	Omura	424/457
6,316,031	11-31-2001	Oshlack, et al.	424/495
6,337,091	01-08-2002	Kim, et al.	424/485
6,342,249	01-29-2002	Wong, et al.	424/473
6,365,196	04-02-2002	Venkatesh, et al.	424/715
6,368,626	04-09-2002	Bhatt, et al.	424/473
6,372,252	04-16-2002	Blume, et al.	424/464
6,375,978	04-23-2002	Kleiner, et al.	424/449
6,387,404	05-14-2002	Oshlack, et al.	424/480
6,395,292	05-28-2002	Peery, et al.	424/422
6,403,120	06-11-2002	Sherman, et al.	424/461
6,416,786	07-09-2002	Mulye, et al.	424/468
6,419,952	07-16-2002	Wong, et al.	424/463
6,419,953	07-16-2003	Qiu, et al.	424/465
6,419,958	07-16-2002	Sherman, et al.	424/489
6,426,091	07-30-2003	Okumura, et al.	424/468
6,437,000	08-20-2002	Mulye	514/647
6,441,038	08-27-2002	Loder, et al.	514/561
6,461,631	10-08-2002	Dunn, et al.	424/426
6,475,521	11-05-2002	Timmins, et al.	424/469
6,491,950	12-10-2002	Gutierrez-Rocca	424/486
6,492,488	12-10-2002	Adams, et al.	528/502
6,495,162	12-17-2002	Cheng, et al.	424/464
6,500,454	12-31-2002	Percel, et al.	424/451
6,602,911	08-05-2003	Kranzler, et al.	514/624

RE 35,601	09-02-1997	Eckenhoff	424/422
RE 37,950	12-31-2002	Dunn, et al.	523/113

Foreign Documents

Number	Publication Date	Patentee	Country
WO 95/22521	08-24-1995	Asahi Chemical Ind.	PCT
WO 97/33880	09-18-1997	Eli Lilly and Co.	PCT
WO 98/08495	03-05-1998	Pierre Fabre Medicament	PCT
WO 00/28980	05-25-2000	Eli Lilly and Co.	PCT
WO 01/26623	04-19-2001	Laxdale Ltd.	PCT
WO 02/060428	08-08-2002	Sepracor, Inc.	PCT

Publications

AL-CHAER, et al., "A new model of chronic visceral hypersensitivity in adult rats induced by colon irritation during postnatal development," *Gastroenterology* 119: 1276-1285 (2000).

ANSEL, et al., eds., Pharmaceutical Dosage Forms and Drug Delivery Systems, 6th ed., Williams & Wilkins: Media, PA (1995).

ANSSEAU, et al., "Controlled comparison of milnacipran and fluoxetine in major depression," *Psychopharmacology* 114: 131-137 (1994).

BEL & ARTIGAS, "Modulation of the extracellular 5-hydroxytryptamine brain concentrations by the serotonin and noradrenaline reuptake inhibitor, milnacipran. Microdialysis studies in rats," *Neuropsychopharmacology* 21(6): 745-754 (1999).

BRILEY, "New hope in the treatment of painful symptoms in depression," *Curr. Opin. Investig. Drugs* 4:42-45 (2003).

BRILEY, et al., "Preclinical pharmacology of milnacipran," *Int. Clin. Psychopharmacology* 11 (Suppl 4): 9-14 (1996).

CACCIA, "Metabolism of the newer antidepressants: an overview of the pharmacological and pharmacokinetic implications," *Clin. Pharmacokinet.* 34(4): 281-302 (1998).

CARON, et al., "Acute electrophysiological effects of intravenous milnacipran, a new antidepressant agent," *Eur. Neuropsychopharmacology* 3: 493-500 (1993).

CHOU & TALALAY, "Quantitative analysis of dose-effect relationships: the combined effects of multiple drugs or enzyme inhibitors," *Adv. Enzyme Regul.* 22: 27-55 (1984).

Cypress Bioscience, Inc., "Cypress Bioscience Inc. announces final results of milnacipran phase II clinical trial in fibromyalgia," March 21, 2003 Media Release, www.cypressbio.com.

DEPREZ, et al., "Which bioequivalence study for a racemic drug? Application to milnacipran," *Eur. J. Drug Metab. Pharmacokinet.* 23(2): 166-171 (1998).

DOYLE & HU, "A new enantioselective synthesis of milnacipran and an analogue by catalytic asymmetric cyclopropanation," *Adv. Synth. Catal.* 343(3): 299-302 (2001).

EISEN, "Venflaxine therapy for vulvodynia," *The Pain Clinic* 8(4): 365-367 (1995).

Eli Lilly & Company, "New research shows cymbalta reduces anxiety symptoms associated with depression," September 18, 2003 Media Release, www.newsroom.lilly.com.

GHEBRE-SELLASSIE, ed., Multiparticulate Oral Drug Delivery, Marcel Dekker, Inc.: New York, NY (1994).

GIAMBERARDINO, "Recent and forgotten aspects of visceral pain," *Eur. J. Pain* 3: 77-92 (1999).

GUELFI, "A double-blind comparison of the efficacy and safety of milnacipran and fluoxetine in depressed inpatients," *Int. Clin. Psychopharmacology* 13: 121-128 (1998).

HINDMARCH, "Do we need new antidepressants?" *Hum. Phsychopharmacol.* 12: 115-119 (1997).

HUFFMAN, et al., "Lithium alkoxides of cinchona alkaloids as chiral controllers for enantioselective acetylide addition to cyclic N-acyl ketimines," *J. Org. Chem.* 60: 1590-1594 (1995).

JACQUES, et al., eds., Enantiomers, Racemates and Resolutions, John Wiley & Sons (1981).

LEINONEN, "Long-term efficacy and safety of milnacipran compared to clomipramine in patients with major depression," *Acta Psychiatr. Scand.* 96: 497-504 (1997).

LIEBERMAN, et al., eds., Pharmaceutical Dosage Form Tablets, Marcel Dekker, Inc.: New York, NY (1989).

LOPEZ-IBOR, et al., "Milnacipran and selective serotonin reuptake inhibitors in major depression," *Int. Clin. Psychopharm.* 11 (Suppl. 4): 41-46 (1996).

MOCHIZUKI, et al., "Neurochemical and behavioural characterization of milnacipran, a serotonin and noradrenaline reuptake inhibitor in rats," *Psychopharmacology* 162: 323-332 (2002).

MORET & BRILEY, "Effects of milnacipran and pindolol on extracellular noradrenaline and serotonin levels in guinea pig hypothalamus," *J. Neurochem.* 69(2): 815-822 (1997).

MORET, et al., "Biochemical profile of midalcipran (F 2207), 1-phenyl-1-diethyl-aminocarbonyl-2-aminomethyl-cyclopropane (Z) hydrochloride, a potential fourth generation antidepressant drug," *Neuropharmacology* 24(12): 1211-1219 (1985).

MUGNAINI, et al., "Receptor binding characteristics of the novel NMDA receptor glycine site antagonist [3H]GV150526A in rat cerebral cortical membranes," *Eur. J. Pharmacol.* 391: 233-241 (2000).

NALIBOFF, et al., "Evidence for two distinct perceptual alterations in irritable bowel syndrome," *Gut* 41: 505-512 (1997).

PALMIER, et al., "Monoamine uptake inhibition by plasma from healthy volunteers after single oral doses of the antidepressant milnacipran," *Eur. J. Clin. Pharmacol.* 37(3): 235-238 (1989).

PUECH, et al., "Milnacipran, a new serotonin and noradrenaline reuptake inhibitor: an overview of its antidepressant activity and clinical tolerability," *Int. Clin. Psychopharmacol.* 12: 99-108 (1997).

PUOZZO & LEONARD, "Pharmacokinetics of milnacipran in comparison with other antidepressants," *Int. Clin. Psychopharmacol.* 11: 15-27 (1996).

PUOZZO, et al., "Pharmacokinetics of milnacipran in renal impairment," *Eur. J. Drug Metab. Pharmacokinetics* 23: 280-286 (1998).

SANCHEZ & HYTTEL, "Comparison of the effects of antidepressants and their metabolites on reuptake of biogenic amines and on receptor binding," *Cell. Mol. Neurobiol.* 19(4): 467-489 (1999).

SCHOEMAKER, et al., "Binding of [3H]ifenprodil, a novel NMDA antagonist, to a polyamine-sensitive site in the rat cerebral cortex," *Eur. J. Pharmacol.* 176: 249-250 (1990).

SHUTO, et al., "(+/-)-(Z)-2-(aminomethyl)-1-phenylcyclopropanecarboxamide derivatives as a new prototype of NMDA receptor antagonists," *J. Med. Chem.* 38: 2964-2968 (1995).

SHUTO, et al., "(1S,2R)-1-Phenyl-2-[(S)-1-aminopropyl]-N,N-diethylcyclopropanecarboxamide (PPDC), a new class of NMDA-receptor antagonist: molecular design by a novel conformational restriction strategy," *Jpn. J. Pharmacol.* 85: 207-213 (2001).

SHUTO, et al., "Synthesis and biological activity of conformationally restricted analogs of milnacipran: (1S,2R)-1-phenyl-2-[(S)-1-aminopropyl]-N,N-diethylcyclopropanecarboxami de, an efficient noncompetitive N-methyl-D-aspartic acid receptor antagonist," *J. Med. Chem.* 39: 4844-4852 (1996).

SHUTO, et al., "Synthesis and biological activity of conformationally restricted analogues of milnacipran: (1S, 2R)-1-phenyl-2-[(R)-1-amino-2-propynyl]-N,N-diethylcyclopropanecarboxamide is a novel class of NMDA receptor channel blocker," *J. Med. Chem.* 41: 3507-3514 (1998).

SHUTO, et al., "Synthesis of (+)- and (-)-milnaciprans and their conformationally restricted analogs," *Tetrahedron Lett.* 37(5): 641-644 (1996).

TALLEY & SPILLER, "Irritable bowel syndrome: a little understood organic bowel disease?" *Lancet* 360: 555-564 (2002).

TIGNOL, et al., "Double-blind study of the efficacy and safety of milnacipran and imipramine in elderly patients with major depressive episode," *Acta Psychiatr. Scand.* 97: 157-165 (1998).

TRAN, et al., "Dual monoamine modulation for improved treatment of major depressive disorder," *J. Clin. Psychopharmacol.* 23: 78-86 (2003).

TUCKER, et al, "Synthesis of a series of 4-(arylethynyl)-6-chloro-4-cyclopropyl-3,4-dihydroquinazolin-2(1H)-ones as novel non-nucleoside HIV-1 reverse transcriptase inhibitors," *J. Med. Chem.* 37: 2437-2444 (1994).

TURCOTTE, et al., "Assessment of the serotonin and norepinephrine reuptake blocking properties of duloxetine in healthy subjects," *Neuropsychopharmacology* 24(5): 511-521 (2001).

VIAZZO, et al., "Microbioligical transformations 34: enantioselective hydrolysis of a key-lactone involved in the synthesis of the antidepressant milnacipran," *Tetrahedron Lett.* 37(26): 4519-4522 (1996).

VON FRENCKELL, et al., "Pooling two controlled comparisons of milnacipran (F2207) and amitriptyline in endogenous inpatients. A new approach in dose ranging studies," *Int. Clin. Psychopharmacol.* 5: 49-56 (1990).

WILDING, "The role of gamma-scintigraphy in oral drug delivery," *Drug Deliv. Rev.* 46: 103-124 (2001).

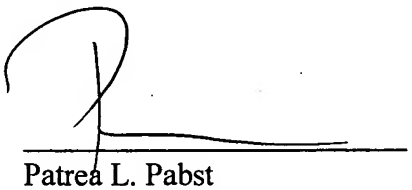
YOSHIMURA, et al., "The involvement of the tetrodotoxin-resistant sodium channel $Na_v1.8$ (PN3/SNS) in a rat model of visceral pain," *J. Neurosci.* 21(21): 8690-8696 (2001).

ZUBAY, Biochemistry, 2nd ed., Macmillan: New York, pp. 259-283 (1988).

Remarks

This statement should not be interpreted as a representation that an exhaustive search has been conducted or that no better art exists. Moreover, Applicants invite the Examiner to make an independent evaluation of the cited art to determine its relevance to the subject matter of the present application. Applicants are of the opinion that their claims patentably distinguish over the art referred to herein, either alone or in combination.

Respectfully submitted,



Patrea L. Pabst
Reg. No. 31,284

Dated: March 3, 2004

HOLLAND & KNIGHT LLP
One Atlantic Center
1201 West Peachtree Street, N.E.
Suite 2000
Atlanta, Georgia 30309-3400
404-817-8473
FAX 404-817-8588
www.hklaw.com

Certificate of Mailing under 37 C.F.R. § 1.8(a)

I hereby certify that this Information Disclosure Statement, along with any paper referred to as being attached or enclosed, is being deposited with the United States Postal Service on the date shown below with sufficient postage as first-class mail in an envelope addressed to the Assistant Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Date: March 3, 2004

Peggy Bailey
SECRETARY

1715422_v1

w.Please type a plus sign (+) inside this box →

PTO/SB/08A (10-96
Approved for use through 10/31/99. OMB 0651-0031
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Complete if Known	
Application Number	10/690,872
Filing Date	October 22, 2003
First Named Inventor	Jane Hirsh
Group Art Unit	
Examiner Name	
Attorney Docket Number	CP 107 P

Sheet	1	of	18

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	US Patent Document Number	Kind Code[2] (if known)	Name of Patentee or Applicant of Cited Document	Date of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		3,948,254		Zaffaroni	04-06-1976	
		3,977,992		Hofacker	08-31-1976	
		4,069,307		Higuchi, et al.	01-17-1978	
		4,093,709		Choi, et al.	06-06-1978	
		4,122,157		Huber	10-24-1978	
		4,138,475		McAinsh, et al.	02-06-1979	
		4,142,526		Zaffaroni	03-06-1979	
		4,173,626		Dempski	11-06-1979	
		4,226,849		Schor	10-07-1980	
		4,249,531		Heller, et al.	02-10-1981	
		4,252,786		Weiss, et al.	02-24-1981	
		4,264,573		Powell, et al.	04-28-1981	
		4,304,232		Michaels	12-08-1981	
		4,308,251		Dunn, et al.	12-29-1981	
		4,322,311		Lim, et al.	05-30-1982	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Office.[3]	Number[4]	Kind Code[5] (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T[6]
		PCT	WO 95/22521		Asahi Chemical Ind.	08-24-1995		
		PCT	WO 97/33880		Eli Lilly and Co.	09-18-1997		
		PCT	WO 98/08495		Pierre Fabre Medicament	03-05-1998		
		PCT	WO 00/28980		Eli Lilly and Co.	05-25-2000		
		PCT	WO 01/26623		Laxdale Ltd.	04-19-2001		
		PCT	WO 02/060428		Sepracor, Inc.	08-08-2002		

Examine Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to application.

[1] Unique citation designation number [2] See attached Kinds of U.S. Patent Documents. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SENT TO: Assistant Commission for Patent, Washington, DC 20231.

Please type a plus sign (+) inside this box →

PTO/SB/08A (10-96
Approved for use through 10/31/99. OMB 0651-0031
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Complete if Known	
Application Number	10/690,872
Filing Date	October 22, 2003
First Named Inventor	Jane Hirsh
Group Art Unit	
Examiner Name	
Attorney Docket Number	CP 107 P

Sheet	2	of	18

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	US Patent Document Number	Kind Code[2] (if known)	Name of Patentee or Applicant of Cited Document	Date of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		4,346,709		Schmitt	08-31-1982	
		4,353,887		Hess, et al.	10-12-1982	
		4,367,741		Michaels	01-11-1983	
		4,415,547		Yu, et al.	11-15-1983	
		4,428,925		Keith	01-31-1984	
		4,428,926		Keith	01-31-1984	
		4,432,965		Keith, et al.	02-21-1984	
		4,455,144		Michaels	06-19-1984	
		4,478,836		Mouzin, et al.	10-23-1984	
		4,482,533		Keith	11-13-1984	
		4,503,031		Glassman	03-05-1985	
		4,505,890		Jain, et al.	03-19-1985	
		4,508,702		Hsiao	04-02-1985	
		4,520,009		Dunn	05-28-1985	
		4,524,060		Mughal, et al.	06-18-1985	
		4,540,566		Davis, et al.	09-10-1985	
		4,556,678		Hsiao	12-03-1985	
		4,557,925		Lindahl, et al.	21-10-1985	
		4,571,333		Hsiao, et al.	02-18-1986	
		4,587,118		Hsiao	05-06-1986	
		4,610,870		Jain, et al.	09-09-1986	
		4,629,619		Lindahl, et al.	12-16-1986	
		4,629,620		Lindahl, et al.	12-16-1986	
		4,634,587		Hsiao	01-06-1987	
		4,649,043		Urquhart, et al.	03-10-1987	

Examine Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to application.

[1] Unique citation designation number [2] See attached Kinds of U.S. Patent Documents. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SENT TO: Assistant Commission for Patent, Washington, DC 20231.

Please type a plus sign (+) inside this box →

PTO/SB/08A (10-98
Approved for use through 10/31/99. OMB 0651-0031
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Complete if Known	
Application Number	10/690,872
Filing Date	October 22, 2003
First Named Inventor	Jane Hirsh
Group Art Unit	
Examiner Name	
Attorney Docket Number	CP 107 P

Sheet 3 of 18

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	US Patent Document Number	Kind Code[2] (if known)	Name of Patentee or Applicant of Cited Document	Date of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		4,666,705		DeCrosta, et al.	05-19-1987	
		4,690,824		Powell, et al.	09-01-1987	
		4,692,337		Ukigaya	09-08-1987	
		4,695,467		Uemura, et al.	09-22-1987	
		4,695,591		Hanna, et al.	09-22-1987	
		4,708,834		Cohen, et al.	11-24-1987	
		4,710,384		Rotman	12-01-1987	
		4,734,285		Alderman	03-29-1988	
		4,740,198		Theeuwes	04-26-1988	
		4,756,911		Drost, et al.	07-12-1988	
		4,775,535		Lowey	10-04-1988	
		4,781,919		Liebowitz	11-01-1988	
		4,784,858		Ventouras	11-15-1988	
		4,795,327		Gaylord, et al.	01-03-1989	
		4,795,642		Cohen, et al.	01-03-1989	
		4,795,645		Friedman, et al.	01-03-1989	
		4,798,725		Patel	01-17-1989	
		4,800,083		Hom, et al.	01-24-1989	
		4,803,076		Ranade	02-07-1989	
		4,803,079		Hsiao, et al.	02-07-1989	
		4,806,359		Radebaugh, et al.	02-21-1989	
		4,816,262		McMullen	03-28-1989	
		4,820,522		Radebaugh, et al.	04-11-1989	
		4,822,619		Eichel, et al.	04-18-1989	
		4,824,678		Lindahl, et al.	04-25-1989	

Examine Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to application.

[1] Unique citation designation number [2] See attached Kinds of U.S. Patent Documents. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SENT TO: Assistant Commission for Patent, Washington, DC 20231.

Please type a plus sign (+) inside this box → [+]

PTO/SB/08A (10-98
Approved for use through 10/31/99. OMB 0651-0031
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Complete if Known	
Application Number	10/690,872
Filing Date	October 22, 2003
First Named Inventor	Jane Hirsh
Group Art Unit	
Examiner Name	
Attorney Docket Number	CP 107 P

Sheet 4 of 18

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	US Patent Document Number	Kind Code[2] (if known)	Name of Patentee or Applicant of Cited Document	Date of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		4,832,957		Dempski, et al.	05-23-1989	
		4,837,032		Ortega	06-06-1989	
		4,842,866		Horder, et al.	06-27-1989	
		4,849,229		Gaylord, et al.	07-18-1989	
		4,861,590		Grodberg	08-29-1989	
		4,863,743		Hsiao, et al.	09-05-1989	
		4,871,548		Edgren, et al.	10-03-1989	
		4,882,167		Jang	11-21-1989	
		4,892,742		Shah	01-09-1990	
		4,900,755		Dempski, et al.	02-13-1990	
		4,919,938		Lovegrove, et al.	04-24-1990	
		4,925,676		Ghebre-Sellassie	05-15-1990	
		4,933,185		Wheatley, et al.	06-12-1990	
		4,946,686		McClelland, et al.	08-07-1990	
		4,956,388		Robertson, et al.	09-11-1990	
		4,966,768		Michelucci, et al.	10-30-1990	
		4,968,509		Radebaugh, et al.	11-06-1990	
		4,983,398		Gaylord, et al.	01-08-1991	
		4,983,400		Dempski, et al.	01-08-1991	
		4,983,401		Eichel, et al.	01-08-1991	
		4,996,060		Eckenhoff, et al.	02-26-1991	
		5,002,774		Agrawal, et al.	03-26-1991	
		5,004,613		Radebaugh, et al.	04-02-1991	
		5,007,790		Shell		
		5,009,895		Lui		

Examine Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to application.

[1] Unique citation designation number [2] See attached Kinds of U.S. Patent Documents. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SENT TO: Assistant Commission for Patent, Washington, DC 20231.

Please type a plus sign (+) inside this box →

PTO/SB/08A (10-96
Approved for use through 10/31/99. OMB 0651-0031
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Complete if Known	
Application Number	10/690,872
Filing Date	October 22, 2003
First Named Inventor	Jane Hirsh
Group Art Unit	
Examiner Name	
Attorney Docket Number	CP 107 P

Sheet 5 of 18

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	US Patent Document Number	Kind Code[2] (if known)	Name of Patentee or Applicant of Cited Document	Date of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		5,015,479		Mulligan, et al.	05-14-1991	
		5,019,398		Daste	05-28-1991	
		5,051,261		McGinity, et al.	09-24-1991	
		5,055,306		Barry, et al.	10-08-1991	
		5,057,318		Magruder, et al.	10-15-1991	
		5,073,380		Babu, et al.	12-17-1991	
		5,075,114		Roche	12-24-1991	
		5,085,865		Nayak	02-04-1992	
		5,091,189		Heafield, et al.	02-25-1992	
		5,112,614		Magruder, et al.	05-12-1992	
		5,126,145		Evenstad, et al.	06-30-1992	
		5,137,727		Eckenhoff	08-11-1992	
		5,162,117		Stupak	11-10-1992	
		5,164,193		Okada, et al.	11-17-1992	
		5,169,642		Brinker, et al.	11-08-1992	
		5,186,930		Kogan, et al.	02-16-1993	
		5,200,193		Radebaugh, et al.	04-06-1993	
		5,204,121		Bücheler, et al.	04-20-1993	
		5,219,572		Sivaramakrishnan	06-15-1993	
		5,230,901		Einig, et al.	06-27-1993	
		5,234,692		Magruder, et al.	08-10-1993	
		5,234,693		Magruder, et al.	08-10-1993	
		5,238,687		Magruder, et al.	08-24-1993	
		5,268,182		Brinker, et al.	12-07-1993	
		5,277,912		Lowe, et al.	01-11-1994	

Examine Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to application.

[1] Unique citation designation number [2] See attached Kinds of U.S. Patent Documents. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SENT TO: Assistant Commission for Patent, Washington, DC 20231.

Please type a plus sign (+) inside this box →

PTO/SB/08A (10-98
Approved for use through 10/31/99. OMB 0651-0031
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Complete if Known	
Application Number	10/690,872
Filing Date	October 22, 2003
First Named Inventor	Jane Hirsh
Group Art Unit	
Examiner Name	
Attorney Docket Number	CP 107 P

Sheet 6 of 18

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	US Patent Document Number	Kind Code[2] (if known)	Name of Patentee or Applicant of Cited Document	Date of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		5,278,201		Dunn, et al.	01-11-1994	
		5,278,202		Dunn, et al.	01-11-1994	
		5,283,065		Doyon, et al.	02-01-1994	
		5,292,533		McMahon, et al.	03-08-1994	
		5,292,534		Valentine, et al.	03-08-1994	
		5,320,616		Magruder, et al.	06-14-1994	
		5,324,519		Dunn, et al.	06-28-1994	
		5,328,697		Raman, et al.	07-12-1994	
		5,334,392		Cuine, et al.	08-02-1994	
		5,334,393		Bougaret, et al.	08-02-1994	
		5,340,849		Dunn, et al.	08-23-1994	
		5,356,635		Raman, et al.	10-18-1994	
		5,358,723		Ghebre-Sellassie	10-25-1994	
		5,362,424		Lee, et al.	11-08-1994	
		5,366,738		Rork, et al.	11-22-1994	
		5,368,859		Dunn, et al.	11-29-1994	
		5,368,862		Colegrove	11-29-1994	
		5,393,765		Infeld, et al.	02-28-1995	
		5,397,574		Chen	03-14-1995	
		5,407,686		Patel, et al.	04-18-1995	
		5,413,572		Wong, et al.	05-09-1995	
		5,419,918		Lundberg	05-30-1995	
		5,424,289		Yang, et al.	06-13-1995	
		5,427,798		Ludwig, et al.	06-27-1995	
		5,427,799		Valentine, et al.	06-27-1995	

Examine Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to application.

[1] Unique citation designation number [2] See attached Kinds of U.S. Patent Documents. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SENT TO: Assistant Commission for Patent, Washington, DC 20231.

Please type a plus sign (+) inside this box → [+]

PTO/SB/08A (10-98
Approved for use through 10/31/99. OMB 0651-0031
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Complete if Known	
Application Number	10/690,872
Filing Date	October 22, 2003
First Named Inventor	Jane Hirsh
Group Art Unit	
Examiner Name	
Attorney Docket Number	CP 107 P

Sheet 7 of 18

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	US Patent Document Number	Kind Code[2] (if known)	Name of Patentee or Applicant of Cited Document	Date of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		5,433,951		Serajuddin, et al.	06-18-1995	
		5,455,046		Baichwal	10-03-1995	
		5,462,747		Radebaugh, et al.	10-31-1995	
		5,466,460		McMahon, et al.	11-14-1995	
		5,484,607		Horacek	01-16-1996	
		5,487,897		Polson, et al.	01-30-1996	
		5,492,700		Ghebre-Sellassie	02-20-1996	
		5,498,422		Nakamichi, et al.	03-12-1996	
		5,500,227		Oshlack, et al.	03-19-1996	
		5,505,962		Sparks	04-09-1996	
		5,508,041		Lee, et al.	04-16-1996	
		5,512,293		Landrau, et al.	04-30-1996	
		5,512,297		Baichwal	04-30-1996	
		5,540,912		Roorda, et al.	07-30-1996	
		5,543,155		Fekete, et al.	08-06-1996	
		5,554,387		Baichwal	09-10-1996	
		5,558,879		Chen, et al.	09-24-1996	
		5,562,915		Lowe, et al.	10-08-1996	
		5,576,021		Andoh, et al.	09-19-1996	
		5,578,321		Sherman	11-26-1996	
		5,582,837		Shell	12-10-1996	
		5,593,694		Hayashida, et al.	01-14-1997	
		5,599,552		Dunn, et al.	02-04-1997	
		5,601,842		Bartholomaeus	02-11-1997	
		5,603,956		Mateescu, et al.	02-18-1997	

Examine Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to application.

[1] Unique citation designation number [2] See attached Kinds of U.S. Patent Documents. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SENT TO: Assistant Commission for Patent, Washington, DC 20231.

Please type a plus sign (+) inside this box → [+]

PTO/SB/08A (10-96
Approved for use through 10/31/99. OMB 0651-0031
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Complete if Known	
Application Number	10/690,872
Filing Date	October 22, 2003
First Named Inventor	Jane Hirsh
Group Art Unit	
Examiner Name	
Attorney Docket Number	CP 107 P

Sheet 8 of 18

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	US Patent Document Number	Kind Code[2] (if known)	Name of Patentee or Applicant of Cited Document	Date of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		5,614,218		Olsson, et al.	03-25-1997	
		5,621,142		Mochizuki, et al.	04-15-1997	
		5,624,683		Andoh, et al.	04-29-1997	
		5,626,874		Conte, et al.	05-06-1997	
		5,630,808		Magruder, et al.	05-20-1997	
		5,643,602		Ulmius	07-01-1997	
		5,645,858		Kotwal, et al.	07-08-1997	
		5,650,170		Wright, et al.	07-22-1997	
		5,654,005		Chen, et al.	08-05-1997	
		5,656,291		Olsson, et al.	08-12-1997	
		5,660,837		Lundquist	08-26-1997	
		5,667,801		Baichwal	09-16-1997	
		5,681,582		Gilis, et al.	10-28-1997	
		5,681,583		Conte, et al.	10-28-1997	
		5,688,530		Bodmer, et al.	11-18-1997	
		5,690,960		Bengtsson, et al.	11-25-1997	
		5,702,716		Dunn, et al.	12-30-1997	
		5,705,190		Broad, et al.	01-06-1998	
		5,707,655		Kanikanti, et al.	01-13-1998	
		5,733,950		Dunn, et al.	03-31-1998	
		5,736,152		Dunn	04-07-1998	
		5,736,159		Chen, et al.	04-07-1998	
		5,739,176		Dunn, et al.	04-14-1998	
		5,744,153		Yewey, et al.	04-28-1998	
		5,759,563		Yewey, et al.	06-02-1998	

Examine Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to application.

[1] Unique citation designation number [2] See attached Kinds of U.S. Patent Documents. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SENT TO: Assistant Commission for Patent, Washington, DC 20231.

Please type a plus sign (+) inside this box → [+]

PTO/SB/08A (10-98
Approved for use through 10/31/99. OMB 0651-0031
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Complete if Known	
Application Number	10/690,872
Filing Date	October 22, 2003
First Named Inventor	Jane Hirsh
Group Art Unit	
Examiner Name	
Attorney Docket Number	CP 107 P

Sheet 9 of 18

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	US Patent Document Number	Kind Code[2] (if known)	Name of Patentee or Applicant of Cited Document	Date of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		5,776,489		Preston, et al.	07-07-1998	
		5,780,044		Yewey, et al.	07-14-1998	
		5,783,212		Fassihi, et al.	07-21-1998	
		5,846,563		Baichwal	12-08-1998	
		5,849,330		Marvola, et al.	12-15-1998	
		5,861,166		Eckenhoff	01-19-1999	
		5,869,100		Horacek	02-09-1999	
		5,874,107		Fischer, et al.	02-23-1999	
		5,879,707		Cartilier, et al.	03-09-1999	
		5,882,682		Rork, et al.	03-16-1999	
		5,885,615		Chouinard, et al.	03-23-1999	
		5,888,533		Dunn	03-30-1999	
		5,900,425		Kanikanti, et al.	05-04-1999	
		5,945,115		Dunn, et al.	08-31-1999	
		5,945,125		Kim	08-31-1999	
		5,980,942		Katzhendler, et al.	11-09-1999	
		5,990,194		Dunn, et al.	11-23-1999	
		6,010,718		Al-Razzak, et al.	01-04-2000	
		6,024,982		Oshlack, et al.	02-15-2000	
		6,027,748		Conte, et al.	02-22-2000	
		6,030,641		Yamashita, et al.	02-29-2000	
		6,030,642		Horacek	02-29-2000	
		6,033,685		Qiu, et al.	03-07-2000	
		6,033,686		Seth	03-07-2000	
		6,046,177		Stella, et al.	04-04-2000	

Examine Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to application...

[1] Unique citation designation number [2] See attached Kinds of U.S. Patent Documents. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SENT TO: Assistant Commission for Patent, Washington, DC 20231.

Please type a plus sign (+) inside this box → [+]

PTO/SB/08A (10-96
Approved for use through 10/31/98. OMB 0651-0031
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Complete if Known	
Application Number	10/690,872
Filing Date	October 22, 2003
First Named Inventor	Jane Hirsh
Group Art Unit	
Examiner Name	
Attorney Docket Number	CP 107 P

Sheet 10 of 18

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	US Patent Document Number	Kind Code[2] (if known)	Name of Patentee or Applicant of Cited Document	Date of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		6,056,977		Bhagwat, et al.	05-02-2000	
		6,066,643		Perry	05-23-2000	
		6,074,669		Nagaprasad, et al.	06-13-2000	
		6,077,538		Merrill, et al.	06-20-2000	
		6,083,533		Cremer	07-04-2000	
		6,090,411		Pillay, et al.	07-18-2000	
		6,093,387		Birbara, et al.	07-25-2000	
		6,099,859		Cheng, et al.	08-08-2000	
		6,099,862		Chen, et al.	08-08-2000	
		6,106,863		Ukigaya, et al.	08-22-2000	
		6,113,938		Chen, et al.	09-05-2000	
		6,120,789		Dunn	09-19-2000	
		6,126,967		Clemente, et al.	10-03-2000	
		6,136,343		Baichwal	10-24-2000	
		6,143,314		Chandrashekar, et al.	11-07-2000	
		6,143,353		Oshlack, et al.	11-07-2000	
		6,149,940		Maggi, et al.	11-21-2000	
		6,150,396		Iyengar, et al.	11-21-2000	
		6,150,410		Engh, et al.	11-21-2000	
		6,156,343		Morita, et al.	12-05-2000	
		6,162,463		Lippa	12-19-2000	
		6,162,466		Licht, et al.	12-19-2000	
		6,174,547		Dong, et al.	01-16-2001	
		6,180,129		Magruder, et al.	01-30-2001	
		6,197,339		Ju	03-06-2001	

Examine Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to application.

[1] Unique citation designation number [2] See attached Kinds of U.S. Patent Documents. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SENT TO: Assistant Commission for Patent, Washington, DC 20231.

Please type a plus sign (+) inside this box → [+]

PTO/SB/08A (10-98
Approved for use through 10/31/99. OMB 0651-0031
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Complete if Known	
Application Number	10/690,872
Filing Date	October 22, 2003
First Named Inventor	Jane Hirsh
Group Art Unit	
Examiner Name	
Attorney Docket Number	CP 107 P

Sheet 11 of 18

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	US Patent Document Number	Kind Code[2] (if known)	Name of Patentee or Applicant of Cited Document	Date of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		6,197,344		Chang, et al.	03-06-2001	
		6,210,714		Oshlack, et al.	04-03-2001	
		6,221,395		Maggi, et al.	04-24-2001	
		6,245,357		Edgren, et al.	06-12-2001	
		6,251,432		Mazer, et al.	06-26-2001	
		6,254,891		Anaebonam, et al.	07-03-2001	
		6,261,583		Dunn, et al.	07-17-2001	
		6,261,601		Talwar, et al.	07-17-2001	
		6,270,799		Siefert, et al.	08-07-2001	
		6,274,171		Sherman, et al.	08-14-2001	
		6,284,275		Chen, et al.	09-04-2001	
		6,303,144		Omura	10-16-2001	
		6,316,031		Oshlack, et al.	11-31-2001	
		6,337,091		Kim, et al.	01-08-2002	
		6,342,249		Wong, et al.	01-29-2002	
		6,365,196		Venkatesh, et al.	04-02-2002	
		6,368,626		Bhatt, et al.	04-09-2002	
		6,372,252		Blume, et al.	04-16-2002	
		6,375,978		Kleiner, et al.	04-23-2002	
		6,387,404		Oshlack, et al.	05-14-2002	
		6,395,292		Peery, et al.	05-28-2002	
		6,403,120		Sherman, et al.	06-11-2002	
		6,416,786		Mulye, et al.	07-09-2002	
		6,419,952		Wong, et al.	07-16-2002	
		6,419,953		Qiu, et al.	07-16-2003	

Examine Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to application.

[1] Unique citation designation number [2] See attached Kinds of U.S. Patent Documents. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SENT TO: Assistant Commission for Patent, Washington, DC 20231.

Please type a plus sign (+) inside this box → [+]

PTO/SB/08A (10-98
Approved for use through 10/31/99. OMB 0651-0031
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Complete if Known	
Application Number	10/690,872
Filing Date	October 22, 2003
First Named Inventor	Jane Hirsh
Group Art Unit	
Examiner Name	
Attorney Docket Number	CP 107 P

Sheet 12 of 18

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	US Patent Document Number	Kind Code[2] (if known)	Name of Patentee or Applicant of Cited Document	Date of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		6,419,958		Sherman, et al.	07-16-2002	
		6,426,091		Okumura, et al.	07-30-2003	
		6,437,000		Mulye	08-20-2002	
		6,441,038		Loder, et al.	08-27-2002	
		6,461,631		Dunn, et al.	10-08-2002	
		6,475,521		Timmins, et al.	11-05-2002	
		6,491,950		Gutierrez-Rocca	12-10-2002	
		6,492,488		Adams, et al.	12-10-2002	
		6,495,162		Cheng, et al.	12-17-2002	
		6,500,454		Percel, et al.	12-31-2002	
		6,602,911		Kranzler, et al.	08-05-2003	
		RE 35,601		Eckenhoff	09-02-1997	
		RE 37,950		Dunn, et al.	12-31-2002	

Examine Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to application.

[1] Unique citation designation number [2] See attached Kinds of U.S. Patent Documents. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SENT TO: Assistant Commission for Patent, Washington, DC 20231.

Please type a plus sign (+) inside this box →

PTO/SB/08A (10-98
Approved for use through 10/31/99. OMB 0651-0031
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Complete if Known	
Application Number	10/690,872
Filing Date	October 22, 2003
First Named Inventor	Jane Hirsh
Group Art Unit	
Examiner Name	
Attorney Docket Number	CP 107 P

Sheet	13	of	18

OTHER ART -- NON PATENT LITERATURE DOCUMENTS			
Examiner's Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T[2]
		AL-CHAER, et al., "A new model of chronic visceral hypersensitivity in adult rats induced by colon irritation during postnatal development," *Gastroenterology* 119: 1276-1285 (2000).	
		ANSEL, et al., eds., Pharmaceutical Dosage Forms and Drug Delivery Systems, 6th ed., Williams & Wilkins: Media, PA (1995).	
		ANSSEAU, et al., "Controlled comparison of milnacipran and fluoxetine in major depression," *Psychopharmacology* 114: 131-137 (1994).	
		BEL & ARTIGAS, "Modulation of the extracellular 5-hydroxytryptamine brain concentrations by the serotonin and noradrenaline reuptake inhibitor, milnacipran. Microdialysis studies in rats," *Neuropsychopharmacology* 21(6): 745-754 (1999).	
		BRILEY, "New hope in the treatment of painful symptoms in depression," *Curr. Opin. Investig. Drugs* 4:42-45 (2003).	
		BRILEY, et al., "Preclinical pharmacology of milnacipran," *Int. Clin. Psychopharmacology* 11 (Suppl 4): 9-14 (1996).	
		CACCIA, "Metabolism of the newer antidepressants: an overview of the pharmacological and pharmacokinetic implications," *Clin. Pharmacokinet.* 34(4): 281-302 (1998).	
		CARON, et al., "Acute electrophysiological effects of intravenous milnacipran, a new antidepressant agent," *Eur. Neuropsychopharmacology* 3: 493-500 (1993).	
		CHOU & TALALAY, "Quantitative analysis of dose-effect relationships: the combined effects of multiple drugs or enzyme inhibitors," *Adv. Enzyme Regul.* 22: 27-55 (1984).	

Examiner's Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] Unique citation designation number [2] See attached Kinds of U.S. Patent Documents. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you require to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

Please type a plus sign (+) inside this box → [+]

PTO/SB/08A (10-98
Approved for use through 10/31/99. OMB 0651-0031
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Complete if Known	
Application Number	10/690,872
Filing Date	October 22, 2003
First Named Inventor	Jane Hirsh
Group Art Unit	
Examiner Name	
Attorney Docket Number	CP 107 P

Sheet 14 of 18

OTHER ART -- NON PATENT LITERATURE DOCUMENTS			
Examiner's Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T[2]
		Cypress Bioscience, Inc., "Cypress Bioscience Inc. announces final results of milnacipran phase II clinical trial in fibromyalgia," March 21, 2003 Media Release, www.cypressbio.com.	
		DEPREZ, et al., "Which bioequivalence study for a racemic drug? Application to milnacipran," *Eur. J. Drug Metab. Pharmacokinet.* 23(2): 166-171 (1998).	
		DOYLE & HU, "A new enantioselective synthesis of milnacipran and an analogue by catalytic asymmetric cyclopropanation," *Adv. Synth. Catal.* 343(3): 299-302 (2001).	
		EISEN, "Venflaxine therapy for vulvodynia," *The Pain Clinic* 8(4): 365-367 (1995).	
		Eli Lilly & Company, "New research shows cymbalta reduces anxiety symptoms associated with depression," September 18, 2003 Media Release, www.newsroom.lilly.com.	
		GHEBRE-SELLASSIE, ed., Multiparticulate Oral Drug Delivery, Marcel Dekker, Inc.: New York, NY (1994).	
		GIAMBERARDINO, "Recent and forgotten aspects of visceral pain," *Eur. J. Pain* 3: 77-92 (1999).	
		GUELFI, "A double-blind comparison of the efficacy and safety of milnacipran and fluoxetine in depressed inpatients," *Int. Clin. Psychopharmacology* 13: 121-128 (1998).	
		HINDMARCH, "Do we need new antidepressants?" *Hum. Phsychopharmacol.* 12: 115-119 (1997).	

Examiner's Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] Unique citation designation number [2] See attached Kinds of U.S. Patent Documents. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you require to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

Please type a plus sign (+) inside this box → [+]

PTO/SB/08A (10-98
Approved for use through 10/31/99. OMB 0651-0031
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				Application Number	10/690,872
				Filing Date	October 22, 2003
				First Named Inventor	Jane Hirsh
				Group Art Unit	
				Examiner Name	
Sheet	15	of	18	Attorney Docket Number	CP 107 P

OTHER ART -- NON PATENT LITERATURE DOCUMENTS			
Examiner's Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T[2]
		HUFFMAN, et al., "Lithium alkoxides of cinchona alkaloids as chiral controllers for enantioselective acetylide addition to cyclic N-acyl ketimines," *J. Org. Chem.* 60: 1590-1594 (1995).	
		JACQUES, et al., eds., Enantiomers, Racemates and Resolutions, John Wiley & Sons (1981).	
		LEINONEN, "Long-term efficacy and safety of milnacipran compared to clomipramine in patients with major depression," *Acta Psychiatr. Scand.* 96: 497-504 (1997).	
		LIEBERMAN, et al., eds., Pharmaceutical Dosage Form Tablets, Marcel Dekker, Inc.: New York, NY (1989).	
		LOPEZ-IBOR, et al., "Milnacipran and selective serotonin reuptake inhibitors in major depression," *Int. Clin. Psychopharm.* 11 (Suppl. 4): 41-46 (1996).	
		MOCHIZUKI, et al., "Neurochemical and behavioural characterization of milnacipran, a serotonin and noradrenaline reuptake inhibitor in rats," *Psychopharmacology* 162: 323-332 (2002).	
		MORET & BRILEY, "Effects of milnacipran and pindolol on extracellular noradrenaline and serotonin levels in guinea pig hypothalamus," *J. Neurochem.* 69(2): 815-822 (1997).	
		MORET, et al., "Biochemical profile of midalcipran (F 2207), 1-phenyl-1-diethyl-aminocarbonyl-2-aminomethyl-cyclopropane (Z) hydrochloride, a potential fourth generation antidepressant drug," *Neuropharmacology* 24(12): 1211-1219 (1985).	
		MUGNAINI, et al., "Receptor binding characteristics of the novel NMDA receptor glycine site antagonist [3H]GV150526A in rat cerebral cortical membranes," *Eur. J. Pharmacol.* 391: 233-241 (2000).	

Examiner's Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] Unique citation designation number [2] See attached Kinds of U.S. Patent Documents. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you require to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

Please type a plus sign (+) inside this box →

PTO/SB/08A (10-96
Approved for use through 10/31/99. OMB 0651-0031
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				Application Number	10/690,872
				Filing Date	October 22, 2003
				First Named Inventor	Jane Hirsh
				Group Art Unit	
				Examiner Name	
Sheet	16	of	18	Attorney Docket Number	CP 107 P

OTHER ART -- NON PATENT LITERATURE DOCUMENTS			
Examiner's Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T[2]
		NALIBOFF, et al., "Evidence for two distinct perceptual alterations in irritable bowel syndrome," *Gut* 41: 505-512 (1997).	
		PALMIER, et al., "Monoamine uptake inhibition by plasma from healthy volunteers after single oral doses of the antidepressant milnacipran," *Eur. J. Clin. Pharmacol.* 37(3): 235-238 (1989).	
		PUECH, et al., "Milnacipran, a new serotonin and noradrenaline reuptake inhibitor: an overview of its antidepressant activity and clinical tolerability," *Int. Clin. Psychopharmacol.* 12: 99-108 (1997).	
		PUOZZO & LEONARD, "Pharmacokinetics of milnacipran in comparison with other antidepressants," *Int. Clin. Psychopharmacol.* 11: 15-27 (1996).	
		PUOZZO, et al., "Pharmacokinetics of milnacipran in renal impairment," *Eur. J. Drug Metab. Pharmacokinetics* 23: 280-286 (1998).	
		SANCHEZ & HYTTEL, "Comparison of the effects of antidepressants and their metabolites on reuptake of biogenic amines and on receptor binding," *Cell. Mol. Neurobiol.* 19(4): 467-489 (1999).	
		SCHOEMAKER, et al., "Binding of [3H]ifenprodil, a novel NMDA antagonist, to a polyamine-sensitive site in the rat cerebral cortex," *Eur. J. Pharmacol.* 176: 249-250 (1990).	
		SHUTO, et al., "(+/-)-(Z)-2-(aminomethyl)-1-phenylcyclopropanecarboxamide derivatives as a new prototype of NMDA receptor antagonists," *J. Med. Chem.* 38: 2964-2968 (1995).	
		SHUTO, et al., "(1S,2R)-1-Phenyl-2-[(S)-1-aminopropyl]-N,N-diethylcyclopropanecarboxamide (PPDC), a new class of NMDA-receptor antagonist: molecular design by a novel conformational restriction strategy," *Jpn. J. Pharmacol.* 85: 207-213 (2001).	

Examiner's Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] Unique citation designation number [2] See attached Kinds of U.S. Patent Documents. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you require to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

Please type a plus sign (+) inside this box →

PTO/SB/08A (10-98
Approved for use through 10/31/99. OMB 0651-0031
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				Application Number	10/690,872
				Filing Date	October 22, 2003
				First Named Inventor	Jane Hirsh
				Group Art Unit	
				Examiner Name	
Sheet	17	of	18	Attorney Docket Number	CP 107 P

OTHER ART -- NON PATENT LITERATURE DOCUMENTS			
Examiner's Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T[2]
		SHUTO, et al., "Synthesis and biological activity of conformationally restricted analogs of milnacipran: (1S,2R)-1-phenyl-2-[(S)-1-aminopropyl]-N,N-diethylcyclopropanecarboxami de, an efficient noncompetitive N-methyl-D-aspartic acid receptor antagonist," *J. Med. Chem.* 39: 4844-4852 (1996).	
		SHUTO, et al., "Synthesis and biological activity of conformationally restricted analogues of milnacipran: (1S, 2R)-1-phenyl-2-[(R)-1-amino-2-propynyl]-N,N-diethylcyclopropanecarboxamide is a novel class of NMDA receptor channel blocker," *J. Med. Chem.* 41: 3507-3514 (1998).	
		SHUTO, et al., "Synthesis of (+)- and (-)-milnaciprans and their conformationally restricted analogs," *Tetrahedron Lett.* 37(5): 641-644 (1996).	
		TALLEY & SPILLER, "Irritable bowel syndrome: a little understood organic bowel disease?" *Lancet* 360: 555-564 (2002).	
		TIGNOL, et al., "Double-blind study of the efficacy and safety of milnacipran and imipramine in elderly patients with major depressive episode," *Acta Psychiatr. Scand.* 97: 157-165 (1998).	
		TRAN, et al., "Dual monoamine modulation for improved treatment of major depressive disorder," *J. Clin. Psychopharmacol.* 23: 78-86 (2003).	
		TUCKER, et al, "Synthesis of a series of 4-(arylethynyl)-6-chloro-4-cyclopropyl-3,4-dihydroquinazolin-2(1H)-ones as novel non-nucleoside HIV-1 reverse transcriptase inhibitors," *J. Med. Chem.* 37: 2437-2444 (1994).	
		TURCOTTE, et al., "Assessment of the serotonin and norepinephrine reuptake blocking properties of duloxetine in healthy subjects," *Neuropsychopharmacology* 24(5): 511-521 (2001).	
		VIAZZO, et al., "Microbioligical transformations 34: enantioselective hydrolysis of a key-lactone involved in the synthesis of the antidepressant milnacipran," *Tetrahedron Lett.* 37(26): 4519-4522 (1996).	

Examiner's Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] Unique citation designation number [2] See attached Kinds of U.S. Patent Documents. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you require to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

Please type a plus sign (+) inside this box →

PTO/SB/08A (10-98
Approved for use through 10/31/99. OMB 0651-0031
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Complete if Known	
Application Number	10/690,872
Filing Date	October 22, 2003
First Named Inventor	Jane Hirsh
Group Art Unit	
Examiner Name	
Attorney Docket Number	CP 107 P

Sheet 18 of 18

OTHER ART -- NON PATENT LITERATURE DOCUMENTS			
Examiner's Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T[2]
		VON FRENCKELL, et al., "Pooling two controlled comparisons of milnacipran (F2207) and amitriptyline in endogenous inpatients. A new approach in dose ranging studies," *Int. Clin. Psychopharmacol.* 5: 49-56 (1990).	
		WILDING, "The role of gamma-scintigraphy in oral drug delivery," *Drug Deliv. Rev.* 46: 103-124 (2001).	
		YOSHIMURA, et al., "The involvement of the tetrodotoxin-resistant sodium channel $Na_v1.8$ (PN3/SNS) in a rat model of visceral pain," *J. Neurosci.* 21(21): 8690-8696 (2001).	
		ZUBAY, Biochemistry, 2nd ed., Macmillan: New York, pp. 259-283 (1988).	

Examiner's Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] Unique citation designation number [2] See attached Kinds of U.S. Patent Documents. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you require to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.